

MODIFIED ULTRAFILTRATION IMPROVES LUNG MECHANICS IN CONGENITAL CARDIAC SURGERY - A FACT OR FUTILE: A PROSPECTIVE, OBSERVATIONAL, SINGLE-CENTER STUDY

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ABSTRACT

Objective: Cardiac surgeries involving cardiopulmonary bypass (CPB) can have adverse effects on patients, potentially increasing morbidity. In infants who possess lower blood volume and are exposed to the more artificial surface and larger prime volumes of the CPB, the harmful effects can be significant. Several studies have indicated that modified ultrafiltration (MUF) may yield beneficial effects in cardiac surgery by reducing inflammatory markers, improving hemodynamics, and decreasing excess body water. Our study seeks to evaluate the impact of MUF on pulmonary mechanics in infants undergoing cardiac surgeries on CPB.

Methods: This prospective, observational, single-center study was conducted on 56 infants with congenital heart disease, who underwent cardiac surgery, followed by CPB, were included in this study. The primary outcomes were oxygen saturation (SPO₂), hemoglobin (Hb), peak inspiratory pressure (P_{peak}), and plateau pressure (P_{plat}). The secondary outcomes were systolic and diastolic invasive blood pressures (IBPs), mean arterial pressure (MAP), mean airway pressure (P_{mean}), static lung compliance (C-stat), dynamic lung compliance (C-dyn), expiratory resistance (Re), and work of breathing (WOB).

Results: A statistically significant increase in SPO₂ (98.7 vs. 99.1), Hb (8.3 vs. 13.3), IBP_{systolic} (85 vs. 90), IBP_{diastolic} (56 vs. 61.4), and MAP (66.4 vs. 73.2) was observed in congenital cardiac surgery and CPB patients after MUF (all p<0.05). A statistically significant post-procedural decline in P_{peak} (18.8 vs. 18.3), P_{plat} (18.4 vs. 18.1), Re (79.8 vs. 78), and WOB (1.4 vs. 1.3) was also observed (all p<0.05). However, no significant pre-procedural versus post-procedural differences were observed in P_{mean}, C-stat, and C-dyn (all p>0.05).

Conclusion: MUF effectively improved lung mechanics, oxygen saturation, myocardial contractility, hematocrit, and hemodynamics, and minimized the blood transfusion requirement after CPB in infants with congenital heart disease. Future studies should reinvestigate these outcomes with a larger sample size for an extended follow-up duration.

Keywords: Modified ultrafiltration, Cardiopulmonary bypass, Lung mechanics, Congenital cardiac disease, Lung function, Heart function, Hemodynamics, hematocrit, Blood transfusion.

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INTRODUCTION

Modified ultrafiltration (MUF) reduces excess accumulation of TBW during cardiopulmonary bypass (CPB) and mitigates the detrimental effects of positive fluid balance on organ homeostasis [1,2]. This technique applies a hydrostatic pressure gradient to eliminate low-molecular-weight substances and water from the patient's body. It aims to improve the circulation of various formed elements, including red blood cells [3]. MUF is often used in pediatric patients, treated with CPB during congenital cardiac surgery. It reduces the incidence and risk of systemic inflammatory response syndrome after cardiac surgery by systematically eliminating pro-inflammatory mediators from the circulation [4]. This procedure leads to a 40% increase in hematocrit after CPB [1]. Recent evidence indicates the role of MUF in minimizing inotrope requirements, reducing mechanical ventilation duration, and enhancing hemodynamic status [5]. Findings in the literature also reveal that patients receiving MUF during CPB experience an increase in diastolic/systolic blood pressure and mean arterial blood pressure [6]. A recent meta-analysis reveals the potential of the MUF procedure to reduce intensive care unit (ICU) stay duration, blood product transfusion requirement, chest tube bleeding, and post-perfusion syndrome occurrences after cardiac surgery [7].

MUF reduces hemodilution by conserving blood cells and can be used in infants after administering conventional ultrafiltration [8]. Of note, MUF is known to reduce operative mortality and morbidity in infants treated with CPB [9]. The use of this technique after CPB termination also improves platelet count, plasma proteins, chest tube output, and respiratory function in pediatric patients [10]. It further assists in improving clinical outcomes and minimizing troponin-T and interleukin-6 levels [11]. The improvements in myocardial and hemodynamic functions after MUF are due to the ability of this procedure to enhance arterial blood pressure, global left ventricular function, cardiac index, systolic arterial pressure, and diastolic and systolic blood pressure [12]. The rationale for using MUF in pediatric patients/neonates is to minimize the risk of CPB-induced pulmonary dysfunction, as indicated by minimized gas exchange, high pulmonary vascular resistance, and compromised pulmonary compliance [13,14]. Several research studies have confirmed the role of MUF in improving static/dynamic lung compliance, minimizing lung injury, and enhancing the overall pulmonary function after cardiac surgery in pediatric patients [15,16].

Scientific literature advocates the role of MUF in minimizing circulatory cytokines and reducing the incidence of multiple organ failure and tissue edema in pediatric patients with a high risk of inflammatory

response after CPB [17]. MUF also minimizes bleeding and increases hemoconcentration in patients after CPB [18]. The CPB in pediatric patients is associated with post-procedural inflammation due to several predominant factors, including hypothermia (extreme degrees), the requirement for complex procedures, prolonged bypass times, hemodilution, and body mass [19]. A significant decline in pulmonary function due to CPB is the result of the inflammatory responses, leading to delays in ICU discharge, prolonged extubation, and disrupted cardiopulmonary interactions [20]. Findings from a range of research studies have revealed the role of MUF in shortening PICU stays and ventilatory courses and improving the lung function of pediatric patients treated with CPB and congenital cardiac surgery [21,22]. The impact of MUF on coagulation factors and inflammatory markers possibly enhances thromboelastography parameters, following CPB, in pediatric patients [23]. However, there is a paucity of data regarding the impact of MUF on invasive blood pressure (IBPs), mean arterial pressure (MAP), oxygen saturation level, hemoglobin (Hb) level, peak inspiratory pressure, plateau pressure, mean airway pressure, static/dynamic lung compliance, expiratory/inspiratory resistance, and work of breathing (WOB). Accordingly, this study aimed to investigate the influence of MUF use on the lung mechanics of infants who underwent congenital cardiac surgery with CPB.

METHODS

Study design and patients

This prospective, observational, single-center study was conducted at Sri Padmavathi Pediatric Heart Centre, Tirupati. A total of 94 infants with congenital heart disease were initially scheduled for cardiac surgery, requiring CPB. Both male and female infants (age < 1 year) were included in this study. A written informed consent for cardiac surgery and CPB was obtained from each subject's legally acceptable representatives, including parents. Of note, patients whose legal guardians did not allow their participation in the study were summarily excluded. Other patients with a pre-existing coagulation disorder, evidence of sepsis or pre-existing pulmonary disease, and prior off-pump surgeries were also not included in this study. Finally, a total of 56 infants were included in this study.

The following were monitored on patients after anesthesia induction: (1) P_{plat} (plateau pressure), (2) Peak airway pressures, (3) Driving pressures, (4) C-stat (static lung compliance), and (5) C-dyn (dynamic lung compliance). The following were monitored during the administration of CPB: (1) CPB time; (2) aortic cross-clamp time; and (3) temperature. The pre-MUF analysis included the following tests: (1) P_{plat} , (2) pulmonary artery pressure (PAP), (3) driving pressure, (4) C-stat, (5) C-dyn, (6) Hb, (7) MAP, and (8) PO_2 (oxygen partial pressure). The post-MUF analysis included the following tests: (1) P_{plat} , (2) PAP, (3) driving pressure, (4) C-stat, (5) C-dyn, (6) Hb, (7) MAP, and (8) PO_2 . All enrolled patients were followed up from anesthesia administration to cardiac surgery, CPB, and post-procedural discharge.

Primary and secondary endpoints

The primary outcomes were oxygen saturation (SPO_2), Hb, P_{peak} (peak inspiratory pressure), and P_{plat} . The secondary outcomes included IBP (IBPs-systolic and diastolic), MAP, P_{mean} (mean airway pressure), C-stat, C-dyn, Re (expiratory resistance), and WOB.

Data collection, sample size calculation, and statistical analysis

The study data were collected on pre-configured case report forms. The sample size was calculated using the following formula [24].

$$\text{Sample size} = \frac{2SD^2(Z_{\alpha/2} + Z_{\beta})^2}{d^2}$$

SD: Standard deviation = 2.2 or 1.8 (from previous studies)

$Z_{\alpha/2} = Z_{0.05/2} = Z_{0.025} = 1.96$ at a type 1 error of 5%

$Z_{\beta} = Z_{0.20} = 0.842$ at 80% power

d = effect size = difference between mean values = 0.9.

The patient data were initially collected on the paper-based case report forms and subsequently transferred to the Microsoft Excel spreadsheet [25]. We utilized descriptive statistics to calculate the means and standard deviations for continuous variables and frequencies, with percentages, for categorical variables [26]. The means, standard deviations, and standard error means of pre- and post-MUF groups were compared by a paired sample t-test [27]. The paired sample correlation test was used to evaluate the correlation coefficient and p-value for each of the 13 comparisons [28]. The paired samples test was used to evaluate the differences in means, standard deviations, and standard error means individually for all comparisons within 95% confidence intervals [29]. The corresponding two-tailed p-values determined the significance levels of these differences. The statistical analyses were undertaken via SPSS version 25.0 (IBM Corp., Somers, NY, USA) [30]. The statistical significance was interpreted by the p-value reference ($p \leq 0.05$) [31].

Written informed consent was obtained from the caretakers and parents of the infants who were included in this study.

RESULTS

Among the 56 infants, 28 were males and 28 were females, and the mean age was 7.5 months. The mean weight of the patients was 6.9 kg. Among the infants, the major congenital cardiac pathology was total anomalous pulmonary venous connection in 13 cases, followed by ventricular septal defect in 12 cases and tetralogy of fallot (TOF) in 10 cases, respectively.

The comparison of hemodynamic variables between pre- and post-MUF is shown in Table 1. There was a significant improvement in the invasive systolic and diastolic blood pressure from pre-MUF to post-MUF, and it was significant ($p=0.001$). In addition, the mean arterial blood pressure (66.3 ± 17.67 vs. 73.2 ± 13.58 mmHg; $p=0.001$) and saturated oxygen (98.7 ± 1.52 vs. $99.1 \pm 0.81\%$; $p=0.02$) increased significantly when compared between pre- and post-MUF.

The comparison of respiratory variables between pre- and post-MUF is shown in Table 2. Post-MUF, there was a significant decline in peak inspiratory pressure (18.3 ± 2.94 vs. 18.8 ± 2.91 cmH₂O; $p=0.02$) and plateau pressure (18.1 ± 3.23 vs. 18.4 ± 3.14 ; $p=0.04$) as compared to pre-MUF. There were no significant changes ($p=0.09$) in mean airway pressure between pre- and post-MUF.

The comparison of lung mechanic variables between pre- and post-MUF is shown in Table 3. There was a significant decline in the WOB when compared between pre-MUF and post-MUF (1.4 ± 0.58 vs. 1.3 ± 0.49 J/min; $p=0.001$). Post-MUF, there was a significant decrease in expiratory resistance (78.0 ± 39.30 vs. 79.8 ± 42.99 cmH₂O/L/s; $p=0.003$) and a significant increase in inspiratory resistance (31.0 ± 31.14 vs. 18.8 ± 6.26 cmH₂O/L/s; $p=0.009$). Meanwhile, there were no significant variations in dynamic lung compliance ($p=0.08$) and static lung compliance ($p=0.07$) when compared between pre- and post-MUF.

Regarding Hb level, there was a significant increase during post-MUF as compared to pre-MUF, and it was significant (13.3 vs. 8.3 g/dL; $p < 0.001$). The results are shown in Fig. 1.

DISCUSSION

The overall findings from this study indicated a statistically significant increase in SPO_2 , Hb, IBP (systolic and diastolic), and MAP in congenital cardiac surgery and CPB patients after MUF. Of note, a statistically significant decline in P_{peak} , P_{plat} , Re, and WOB was observed post-MUF in the treated patients. In addition, no significant pre-procedural versus post-procedural differences were observed in P_{mean} , C-stat, and Cdyn.

The improvement in SPO_2 concurs with the literature findings that advocate the enhancement in the gas exchange capacity and subsequent increase in SPO_2 after MUF [16]. Of note, SPO_2 enhancement

Table 1: Comparison of hemodynamic variables between pre- and post-MUF

Parameters	Pre-MUF	Post-MUF	p-value
Invasive systolic BP (mmHg)	85±19.94	90.5±18.24	0.001*
Invasive diastolic BP (mmHg)	56±15.73	61.4±11.86	0.001*
Mean arterial blood pressure (mmHg)	66.3±17.67	73.2±13.58	0.001*
Oxygen saturation (%)	98.7±1.52	99.1±0.81	0.02*

The data were represented as mean±SD. The comparison was made between pre- and post-MUF (paired sample T test). *denotes statistically significant, P<0.05

Table 2: Comparison of respiratory variables between pre- and post-MUF

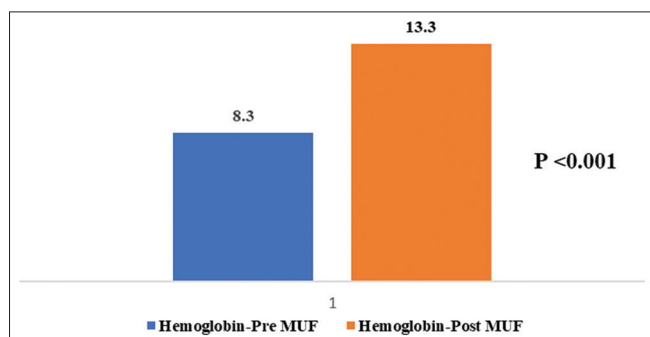
Parameters	Pre-MUF	Post-MUF	p-value
Peak inspiratory pressure (cmH ₂ O)	18.8±2.91	18.3±2.94	0.02*
Plateau pressure (cmH ₂ O)	18.4±3.14	18.1±3.23	0.04*
Mean airway pressure (cmH ₂ O)	8.3±1.25	8.4±1.17	0.09 ^{NS}

The data were represented as mean±SD. The comparison was made between pre- and post-MUF (paired sample t-test). *denotes statistically significant, P<0.05. NS: Non-significant

Table 3: Comparison of lung mechanic variables between pre- and post-MUF

Parameters	Pre-MUF	Post-MUF	p-value
Work of breathing (J/min)	1.4±0.58	1.3±0.49	0.001*
Dynamic lung compliance (ml/cm H ₂ O)	2.2±1.33	2.3±1.32	0.08 ^{NS}
Expiratory resistance (cm H ₂ O/L/s)	79.8±42.99	78.0±39.30	0.003*
Inspiratory resistance (cm H ₂ O/L/s)	18.8±6.26	31.0±31.14	0.009*
Static lung compliance (L/cm H ₂ O)	2.4±1.79	2.4±1.73	0.07 ^{NS}

The data were represented as mean±SD. The comparison was made between pre- and post-MUF (paired sample T test). *denotes statistically significant, P<0.05. NS: Non-significant

**Fig. 1: Comparison of hemoglobin level between pre and post MUF**

after CPB is necessary to maximize the delivery of cerebral oxygen or oxygen-carrying capacity, consequentially improving cardiopulmonary outcomes [32]. An improved SPO₂ is also the outcome of hematocrit improvement. The clearance of dilutional volume through MUF also leads to enhancements in coagulation factors. Alternatively, literature findings also reveal possible reductions in venous oxygen saturation and cerebral blood flow in infants based on an intracranial circulation disruption due to elevated aortic runoff [33]. This complication often occurs during MUF in patients with a diagnosis of dysfunctional cerebral autoregulation.

Our results regarding Hb improvement in patients with MUF match the outcome from a meta-analysis by Hu *et al.* [8], indicating the role of this procedure in increasing post-operative hematocrit or Hb. This outcome relates to the body water elimination capacity of MUF, leading to an increase in red blood cell/hematocrit levels. The hematocrit improvement subsequently reduces the risk of post-procedural dilutional coagulopathy in infants. Furthermore, MUF minimizes the blood cell transfusion requirement by maintaining hemodilution within its safe limit in infants undergoing congenital cardiac surgery (i.e., ≥ 7 g/dL) [34].

Findings from this study regarding the increase in IBP (systolic and diastolic) match the outcomes from a retrospective study by Takabayashi *et al.* [35], indicating instant hematocrit and blood pressure elevation following MUF with CPB. However, literature results do not signify the possible impact of MUF-based blood pressure increases on hemoconcentration and hematocrit in infants treated with congenital cardiac surgery. Similarly, findings concerning MAP elevation concord with the outcomes from a retrospective study by Mohammad, [36] that advocate the role of MUF-based blood conservation protocols in increasing MAP after CPB.

The current findings show a decrease in Re similar to the randomized controlled study of Huang *et al.* [37], which revealed a significant reduction in airway resistance in patients who underwent MUF after CPB. Alternatively, findings from a study by Talwar *et al.* [11] indicated an increase in the peak airway pressure in patients with TOF treated with MUF. The current result, indicating a low P_{peak} after MUF, matched the outcome of a retrospective study by Özdemiş [38]. The possible causes of reduced P_{peak} following MUF include early improvement in pulmonary function, minimization of lung injury, and enhanced static/dynamic pulmonary compliance.

The current findings concerning the decline in P_{plat}, Re, and WOB concurred with the results of Meliones *et al.* [39], Torina *et al.* [40], and Elayashy *et al.* [41]. The possible causes of a decline in airway resistance and breathing efforts in patients undergoing MUF include elevated inspiratory pressure, improved ventilation, and an enhanced lung score. Other potential factors include improved gas exchange, reduced lung congestion, and low pulmonary circulation overload [41]. Contrary to the literature findings, MUF had no statistically significant impact on P_{mean}, C-stat, and Cdyn [39]. Alternatively, the rationale behind the possible influence of MUF on lung mechanics is the potential of this procedure to minimize inflammatory reactions and remove excess water [6,8,40]. Of note, this technique also assists in recovering vena cava blood (~70 mL), which consequentially improves pulmonary circulation [42].

Limitations

This study has several potential limitations that could impact the generalizability of its outcomes across infants treated with MUF after CPB for congenital heart disease. First, the absence of a control group and the lack of randomized sampling reduced the reliability of the results and added to the risk of bias. Second, a small sample size restricted the applicability of outcomes to larger patient populations. Third, this study did not evaluate the impact of comorbidities, prior surgeries, and concomitant or ongoing treatments on the outcomes of MUF in congenital cardiac surgery patients. Finally, the post-procedural data were obtained immediately after performing the MUF intervention. Eventually, the absence of follow-up results impacted the validity of the overall outcomes.

CONCLUSION

The increase in SPO₂ after MUF in the current study indicated improvements in oxygen-carrying capacity and gas change in the lungs of the treated patients. An improvement in Hb levels indicated a reduced blood transfusion requirement. Alternatively, elevations in IBP and MAP were indicative of increased myocardial contractility. The

decline in P_{peak} , P_{plat} , Re, and WOB revealed substantial improvements in lung mechanics after MUF. Together, these results indicated possible improvements in hemodynamics, hematocrit, and overall lung function in infants treated with MUF following CPB. However, no impact of MUF on static lung compliance in patients warrants further assessment, with a larger sample size, by prospective studies.

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CONTRIBUTION OF AUTHORS

Dr. Madhu A. Yadav is involved in the collection of articles, discussion, manuscript writing, and final editing of the manuscript. Dr. Valaji Joshna is involved in the collection of articles, manuscript writing, and statistical analysis. Dr. Srinath Reddy and Dr. Ganapathy Subramanian are involved in the final screening of articles, editing, and proofreading.

CONFLICT OF INTEREST

Nil.

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